FIBRO-ELASTOSIS OF THE HEART IN ADOLESCENCE

BY

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Heart failure in young subjects, when unaccompanied by signs of congenital abnormality or rheumatic disease, can pose a diagnostic problem that may remain unsolved even after careful pathological study. A proportion of such cases in infancy is caused by endocardial fibro-elastosis (Prior and Wyatt, 1950; Dennis *et al.*, 1953), and it has even been suggested that this is one of the commonest types of fatal heart disease in the first year of life (Blumberg and Lyon, 1952). Diagnosis during life is often difficult and the possibility of survival into late childhood or adolescence must be considered when any case of heart disease of unknown ætiology is discovered at this age. Gowing (1953) and Elster *et al.* (1955) have both stated that such cases are not to be found, and that their absence in this intermediate age group suggests that the infantile condition is not ætiologically related to any form of idiopathic heart disease in adults. However, Thomas *et al.* (1954) have published a group of five acceptable and uncomplicated cases, ranging in age from 5–16 years, that were pathologically indistinguishable from the infantile form of the disease, and occasional reports of others, probably similar, have appeared during the last fifty years which suggest that, though rare, survival may occur (Table I). It is interesting that the cases described by Thomas *et al.* had all previously been reported as examples of "idiopathic" heart disease.

TABLE I

CASES PRESENTING IN CHILDHOOD AND ADOLESCENCE, SHOWING CARDIAC LESIONS MORPHOLOGICALLY RESEMBLING THOSE OF INFANTILE FIBRO-ELASTOSIS

Author	Age at death (years)	Remarks
Mahon (1936)	2½	
Vulliamy (1947)	2¾	No reference to elastic stains
Michaud (1906)	3	No reference to elastic stains
Thomas *et al.* (1954), Case 5	5	
Peale and Lucchesi (1942)	5	Complicated by measles, encephalitis, and gonococcal pyosalpinx
Thomas *et al.* (1954), Case 6	6	
Kugel and Stoloff (1933)	6	No reference to elastic stains
Thomas *et al.* (1954), Case 7	7	
Thomas *et al.* (1954), Case 8	11	
Blumberg and Lyon (1952)	11	
Watt and Lynch (1956)	12	Associated with periarteritis nodosa: authors do not consider it of congenital origin
Fowler (1947)	14	No reference to elastic stains
Present case	15	
Thomas *et al.* (1954), Case 9	16	

The following boy with cardiac failure of obscure origin, whose electrocardiogram suggested extensive myocardial infarction, showed at autopsy many of the features of congenital endocardial fibro-elastosis.

Clinical History. A boy of 13 had always appeared healthy. He was the eldest of five brothers and two sisters. He came from a broken home and for three years before admission had been in a residential school for juvenile delinquents, where he seemed fit and able for the rough and tumble of institutional life and organized games.

While playing football he collapsed and was carried off the field. He had felt dizzy just before this, but apart from a few days' constipation had no other complaints. That evening he had vague abdominal pains, and though apyrexial, had several attacks of diarrhœa and vomiting during the night. The following day he developed a mild pyrexia (100° F.), which, with the diarrhœa and vomiting, persisted for four days. He was treated with penicillin by injection and after two weeks was fit to be sent on sick leave. While on holiday a local practitioner suggested a few days' rest in bed and advised him to take things very quietly. On his return to school he looked ill and was tired and listless in spite of long nights in bed. Three days later, whilst trying to run with other boys, he became acutely breathless and dizzy, was admitted to the school sanatorium, and found to be suffering from congestive heart failure, one month after his first collapse.

On admission he was tired and ill, with slight cyanosis, distended neck veins, obvious orthopnœa, and gross pitting œdema of feet, ankles, and shins. There was sinus tachycardia at 108 a minute and the blood pressure was 90/60 mm. Hg. The apex beat, slightly thrusting, was visible in the fifth left interspace half an inch outside the mid-clavicular line. There was gallop rhythm with poor quality heart sounds, a soft apical systolic murmur, and the pulmonary second sound was loud and split. Fine crepitations were present at both lung bases, but there was no enlargement of the liver or spleen and no retinopathy. Heart screening showed generalized cardiac enlargement of moderate degree, and the cardiogram showed an extensive anterior transmural infarct pattern, which from the ST–T wave segments appeared to be in a healing phase (Fig. 1). The most extensive biochemical, bacteriological, and clinico-pathological investigations were carried out and were all normal. No family history of cardiac or other significant illness was obtained. The mother, father, and two siblings were examined fully, and no abnormality was found.

The congestive heart failure responded very slowly to treatment, and after four months in hospital he was discharged on a low salt diet and a maintenance dose of digitalis. Despite greatly restricted activity the congestive failure recurred after three weeks and he was re-admitted to hospital in January, 1954. The clinical picture was much as before, and further investigations threw no new light on the ætiology. A cardiogram showed only minor changes associated with healing of the previously diagnosed infarct (Fig. 1).

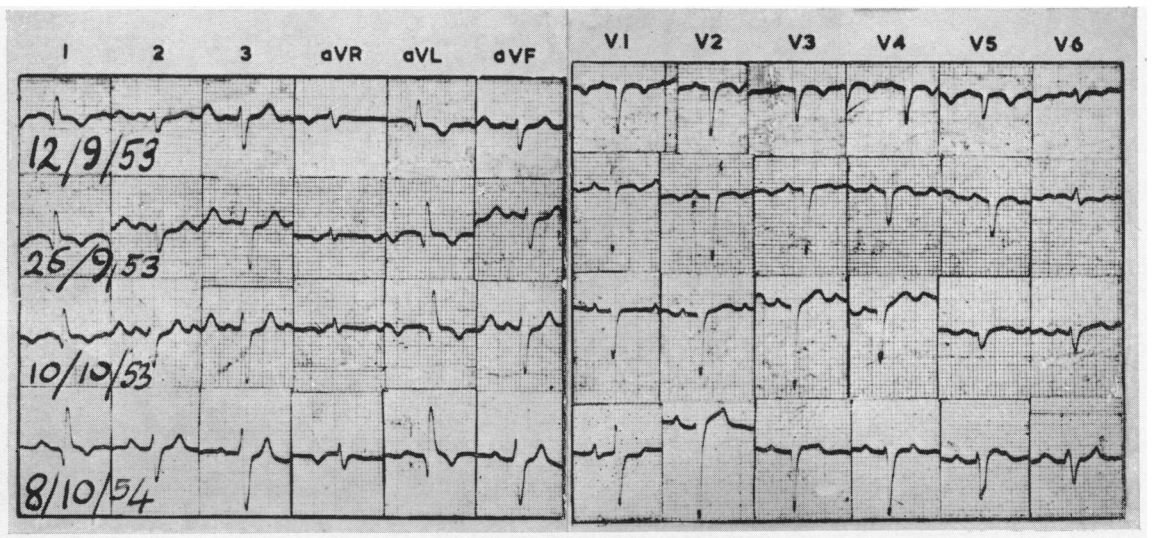

FIG. 1.—Electrocardiograms, showing the pattern of an extensive anterior transmural infarct.

Response to treatment was again slow and a further four months elapsed before he was fit to go back to school. This time, however, he was better than previously and able for moderate activity. He continued on a low salt intake and maintenance dose of digitalis and was seen every two weeks for the next seven months, during which time his condition did not change. In December, 1954, he went to live in another district and one month later his congestive heart failure returned. He was admitted to another hospital in January, 1955, but failed to respond to treatment and gradually deteriorated, dying suddenly two months later.

Necropsy Findings. The main findings were related to the heart. The pericardial sac was healthy. The heart was normal in shape but was considerably enlarged, weighing 525 g. Some patchy areas of pallor were noted in the epicardium on the anterior aspect of the left ventricle. All chambers were dilated especially the left ventricle, the internal measurements of which were $9 \times 7 \times 5$ cm. The left ventricular wall measured 13 mm., the right 7 mm. in thickness. Both atrio-ventricular rings were dilated but the cusps were normal and the pulmonary and aortic valves were healthy. There was no septal abnormality. Pale areas of fibrosis were found throughout the anterior wall of the left ventricle especially in the subendocardial region. The wall was thinned in this part and a large mural thrombus was present over part of the affected area (Fig. 2). Elsewhere the myocardium was of a healthy brown colour. The endocardium in the left ventricle

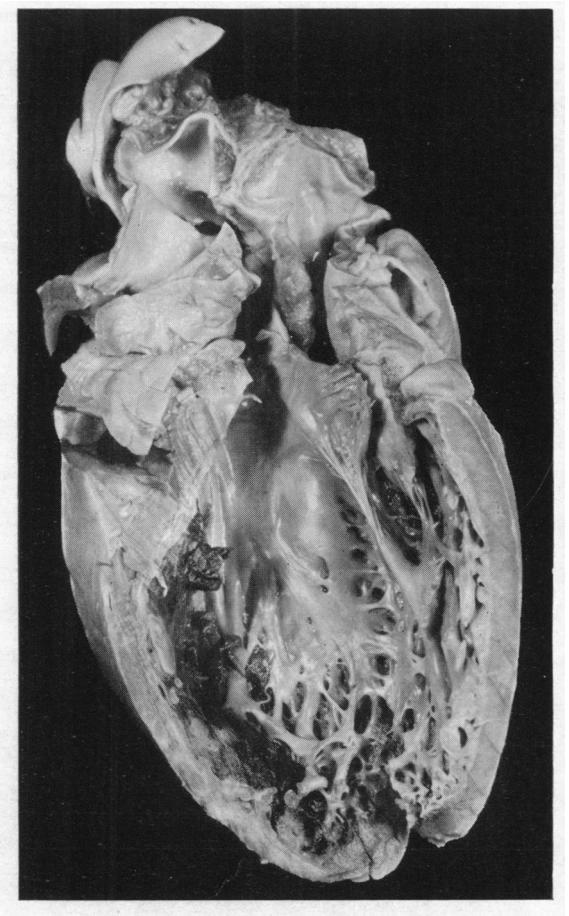

FIG. 2.—The left ventricle viewed from the front. The cut surfaces show the thickened white endocardium with overlying mural thrombus.

was for the most part opaque and white, especially on the anterior and lateral walls of the chamber. The thickened areas merged gradually into normal endocardium at their margins. Similar though slighter endocardial changes were found in the right ventricle, mainly on the septal wall and throughout both atria.

The pulmonary trunk was wider than the aorta, the respective diameters being 20 mm. and 16 mm. Both coronary arteries arose from the aorta, and their ostia were fully patent: the left orifice was elliptical in shape with a mean diameter of 2·5 mm.; the right measured 4·2 mm., and the sum of these diameters was within normal limits. The left coronary artery was of a smaller calibre than the right but both vessels and their main branches were entirely healthy; in particular no atheroma or thrombus formation was demonstrated in a meticulous dissection. Apart from some early atheromatous lesions in its first few centimetres the aorta was of normal appearance. The ductus arteriosus was closed.

Other Findings. Both pleural cavities contained straw-coloured effusions and there was gross ascites. The lungs were firm and congested. The right lower lobe contained three hæmorrhagic infarcts with reddish-brown ante-mortem thrombus in a branch of the pulmonary artery. In the brain a small yellow area of softening about 2 cm. in diameter was present in the cortex of the right parietal lobe. The liver was of normal size but showed nutmeg changes characteristic of chronic venous congestion. The spleen and kidneys were congested in appearance and in the right kidney two small depressed scars resembling healed infarcts were found. There was no evidence of primary renal disease. The left femoral vein was occluded by ante-mortem thrombus.

Histological Findings. A conspicuous abnormality in the wall of the left ventricle took the form of a pronounced fibrous thickening of the endocardium. This extended over much of the interior of the chamber, investing the papillary muscles and sometimes dipping into crypts in the myocardium. Special stains showed that this layer had a rich content of elastic tissue (Fig. 3). Although this fibro-elastic thickening

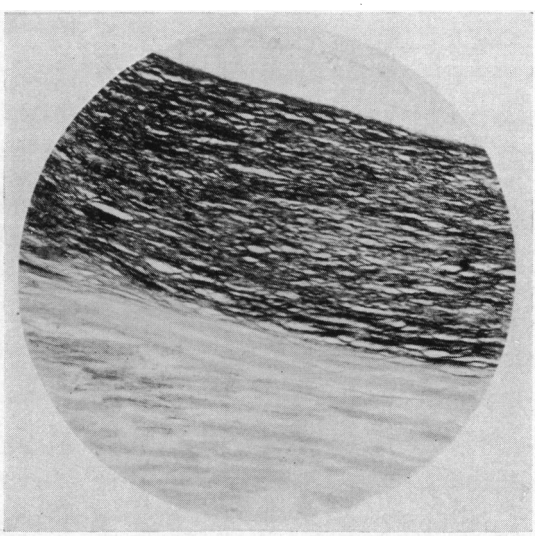

FIG. 3.—Thickened endocardium of the left ventricle, showing proliferation of elastic tissue, with subjacent fibrosis of the myocardium. Orcein, ×55.

was most conspicuous in the left ventricle it was also present to a variable degree in the right ventricle and in both atria. Superficial to the thickened endocardium in the left ventricle the mural thrombus showed varying degrees of organization. In its deeper layers it consisted largely of loose, rather vascular fibro-cellular tissue (Fig. 4).

Numerous zones of interstitial fibrosis, often confluent, were present in the myocardium of the left ventricle. Anteriorly these were scattered throughout the whole thickness of the ventricular wall. In the lateral wall the fibrosis was mainly subendocardial in situation. Similar though less pronounced changes were found in other areas of the heart, notably in the wall of the right atrium and right ventricle (Fig. 5 and 6). Some of these areas of scarring showed a variable admixture with elastic tissue. The muscle fibres, particularly in the neighbourhood of these lesions, were hypertrophied, and often contained large, aberrant hyperchromatic nuclei (Fig. 7). No foci of recent myocardial necrosis were present nor any significant cellular infiltrate in the myocardium. Sections of the heart valves showed no significant abnormality.

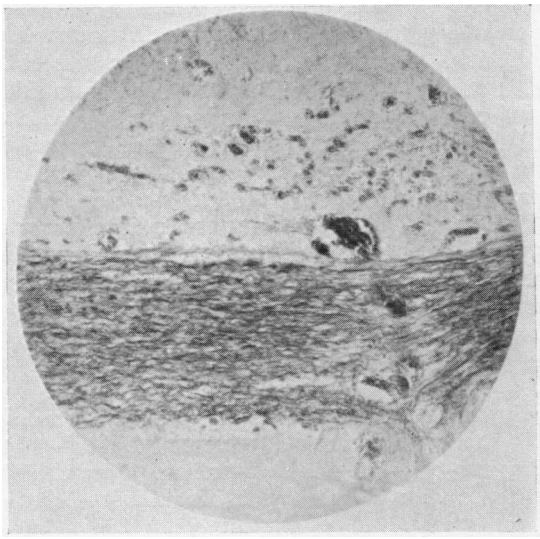

FIG. 4.—Organizing mural thrombus superimposed on fibro-elastosis of the endocardium. Orcein, ×55.

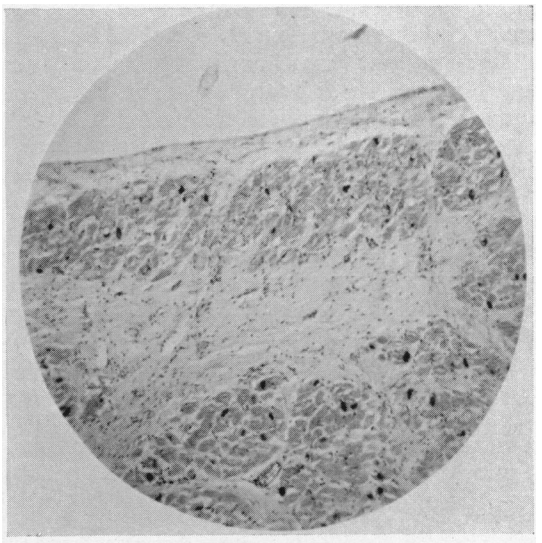

FIG. 5.—Interstitial fibrosis of the myocardium of the right atrium. Hæmatoxylin and eosin, ×55.

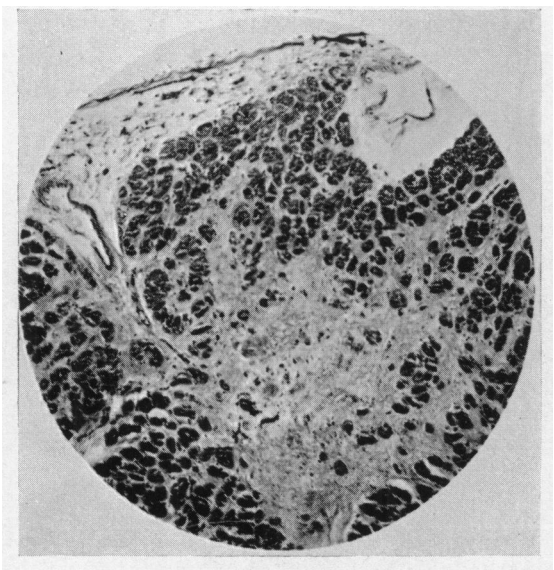

FIG. 6.—Interstitial fibrosis of the myocardium of the right ventricle. Masson's trichome, ×55.

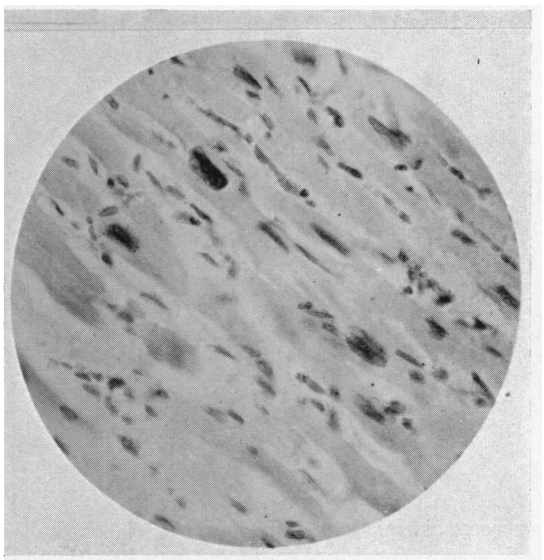

FIG. 7.—Left ventricle. The myocardial fibres are hypertrophied and show large aberrant muclear formations. Hæmatoxylin and eosin, ×240.

The coronary arteries examined at many levels showed no evidence of occlusion. They were indeed entirely healthy in appearance with a single exception of one small arteriole in the wall of the left ventricle which exhibited only a comparatively slight thickening of its intima.

The salient features in other organs were organizing thrombus in branches of the right pulmonary artery with pulmonary infarction; chronic venous congestion of the lungs, liver, spleen, and kidneys; infarcts of considerable duration in the brain and right kidney. Sections from the various organs showed no evidence of any condition belonging to the group of collagen diseases.

Discussion

Cardiac failure of obscure ætiology occurring in young or middle-aged adults, though rare in this country, is not uncommonly reported from America, the European continent, and Africa. If cases showing unexplained inflammatory lesions of the myocardium, as in so-called isolated or Fiedler's myocarditis, are excluded, an apparently miscellaneous group remains in which cardiac hypertrophy has been the common feature. Opinions about ætiology have ranged from dietary deficiencies, antecedent inflammations, etc., to disturbances of collagen metabolism, and the condition has been described by various names (Comeau, 1937; Reisenger and Blumenthal, 1941; Smith and Furth, 1943; Sellars and Phillips, 1946; Ware and Chapman, 1947; Davies *et al.*, 1951; Becker *et al.*, 1953; Thomas *et al.*, 1954; Elster *et al.*, 1955).

This disease group probably includes several distinct syndromes. The endomyocardial fibrosis reported from Africa (Williams *et al.*, 1946) differs in important respects from that seen in America, though a rather similar type has been described in Europe (Löffler, 1936). A few cases, some of sudden death without antecedent illness, probably form another group, in which massive cardiac hypertrophy is the only abnormality (Laubry and Walser, 1925; Whittle, 1929; Reifenstein and Chidsey, 1945). A familial tendency has occasionally been demonstrated (Evans, 1949) and some of these may be related to Friedreich's ataxia. Some can no longer be regarded as idiopathic; examples of glycogen disease affecting the heart have been included in earlier series (Levy and von Glahn, 1944), and mention of coronary arterial disease in other cases raises doubt about the alleged idiopathic nature of the myocardial or endocardial changes described.

Many, however, remain unclassified and no sharp differentiation is possible on either clinical or pathological grounds. They are usually men in the second to fifth decade presenting with symptoms of congestive heart failure often of short duration. The illness commonly runs a rapid downhill course and death may occur within a few months of the appearance of symptoms. At autopsy the heart is always enlarged, and may show varying degrees of endocardial and/or myocardial involvement, ranging from minor degenerative changes in the deeper layers of the myocardium (Reisenger and Blumenthal, 1941) to a picture of diffuse endocardial fibrosis, mural thrombus formation with multiple infarction in the viscera, and extensive fibrosis throughout the myocardium easily visible macroscopically (Smith and Furth, 1943; Ware and Chapman, 1947). All intervening grades of endocardial thickening and interstitial fibrosis and scarring may be seen. According to Fowler (1947), there is a progressive fibrosis of the heart from within outwards. A tendency for the subendocardial zone to be most affected is frequently noted, the left ventricle usually being involved.

In many respects, the morphological appearances resemble those of congenital fibro-elastosis, and on the few occasions when special staining methods have been used, a rich content of elastic fibres has been demonstrated in the thickened endocardium (Comeau, 1937; Elster *et al.*, 1955). In their 12 adult cases of chronic heart disease of obscure ætiology, aged 16 and upwards, Thomas *et al.* (1954) demonstrated abnormal degrees of endocardial fibro-elastosis and reached the conclusion that the lesion was congenital and of essentially the same nature as the infantile form. It is doubtful whether this conclusion is applicable to all adolescent and adult cases of idiopathic heart disease of the type just reviewed, but it certainly deserves serious consideration in the present case. The finding of extensive interstitial fibrosis does not appear to invalidate this opinion, and has already been reported in children with fibro-elastosis, e.g. in Thomas *et al.*, Case 7, where it was originally regarded as the essential lesion. The natural evolution of fibro-elastosis of the endocardium over a period of years in a surviving child cannot be defined until a thorough examination of many more hearts has been made, paying particular attention to the content and distribution of elastic tissue and concomitant interstitial fibrosis. The fibrosis may well be a sequel to the hypertrophy, for as pointed out by Roberts and Wearn (1941), increased muscle mass in cardiac hypertrophy may exceed the functional capacity of the capillaries thus impairing its metabolism. It is also possible that the myocardial changes observed in fibro-elastosis may be initiated by obliteration of the Thebesian vessels owing to the elastic thickening of the endocardium, as suggested by Gross (1941) and Halliday (1954).

The electrocardiogram in this case, showing the pattern of extensive transmural infarction, is of special interest and importance in view of the absence of coronary artery disease. Though conduction defects, arrhythmias, and ST–T wave changes are common in fibro-elastosis, we have been unable to find any other case of this disease or of heart disease of unknown ætiology in which cardiographic changes of the present type are reported or illustrated. For this reason the possibility of fibro-elastosis was not considered during life when the problem of ætiology arose. It is stressed now, not as a common or likely cause of an infarct pattern, but as a diagnosis that should be considered when this pattern is obtained from a young patient. While the cardiogram was characteristic of an infarction, the exact date of the onset of the lesion could not be determined. The first record suggested that it was of some weeks' standing, and in the chest leads the changing T waves during his first admission, compatible with healing myocardial damage, suggested that an active process was then taking place in the myocardium. Its exact nature, however, is obscure. Evidently in the process of establishing the sequence of the pathological changes in fibro-elastosis of the endocardium in surviving children and adolescents, it will be necessary to correlate them more and more precisely with the corresponding electrocardiograms.

SUMMARY

A small group of reported cases has been abstracted to provide evidence that some patients with congenital endocardial fibro-elastosis may survive beyond infancy. The case is described of a youth, aged 15, who died in congestive heart failure. Post mortem, the heart was enlarged and showed well-marked endocardial fibro-elastosis, with mural thrombus formation and myocardial fibrosis.

The pathogenesis of the case is discussed in relation to congenital fibro-elastosis and to idiopathic heart disease in adults. The electrocardiograms were of unusual interest in showing the pattern commonly associated with extensive transmural myocardial infarction.

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